UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

EPA United States Environmental Protection Agency Office of Pesticide Programs

MEMORANDUM

7/28/2020

SUBJECT: Acute Toxicity Review for Neogen Viroxide Super, EPA Reg. No.: 66171-RNA

FROM: Milutin S. Djurickovic 07/28/2020
Risk Assessment Branch
Biopesticides Pollution Prevention Division

THRU: Jenny J. Tao, Senior Scientist (Acute Toxicology) 07/28/2020
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

TO: Jacqueline Hardy, PM Team 34 / Karen Leavy
Regulatory Management Branch I
Antimicrobials Division (7510P)

Registrant: Preserve International		
Decision No.: 562503	Submission No.: 1051299	E-Sub No.: 49751
DP No.: 458034	Action Code: A572	
MRID No(s).: 50934826 to 50934831		

Formulation from label			
PC code(s)	CAS #(s)	Active Ingredient(s)	% weight
013905 063604	10058-23-8 7647-14-5	Potassium peroxymonosulfate Sodium Chloride	22.41 1.50
		Other Ingredients	76.09
		Total	100%

I. BACKGROUND

The Registrant, Preserve International, has submitted an application for pesticide registration for their product: *Neogen Viroxide Super*, EPA Reg. No. 66171-RNA. The proposed product contains the active ingredients Potassium peroxymonosulfate and Sodium Chloride (a.i.), chemical CAS No's 10058-23-8 and 7647-14-5. The registrant states that the new a.i.'s in *Neogen Viroxide Super* are "very similar" to the existing a.i.'s in EPA Reg. No. 39967-137. To address the acute toxicity data requirements, the registrant has provided all the required studies. The proposed product is a broad spectrum disinfectant designed for aquaculture, greenhouses, animal production facilities, and food or meat processing plants.

II. FINDINGS/RECOMMENDATIONS

1. Acute Oral Toxicity

The submitted study report (MRID 50934826) indicated that no animals survived the limit dose of 5000 mg/kg bw. The Main Test resulted in an estimated LD_{50} of 3129 mg/kg, placing the proposed product in Toxicity Category III. The study is acceptable.

2. Acute Dermal Toxicity

A study (MRID 50934827) was submitted. No mortalities occurred and there were no abnormal gross necropsy findings, and all animals gained weight during both weeks of the study. Abnormal clinical signs were limited to local effects on all dose sites. The study is acceptable, and Toxicity Category IV is assigned.

3. Acute Inhalation Toxicity

The submitted study report (MRID 50934828) reported a LC50 > 0.56 mg/L and < 2.20 mg/L. At 0.56 mg/L no mortalities occurred with irregular respiration on day 1 and no gross abnormal necropsy findings. At 2.20 mg/L one animal died while all of the others were sacrificed for humane reasons. All animals exhibited irregular respiration and moist rales (first noted upon removal from the chamber), followed by gasping and/or hypoactivity (first noted Day 1), with red facial staining noted on two males. At necropsy, all animals had distension of the stomach and intestines and red discoloration of the lungs classifying the proposed product as Toxicity Category III. The study is acceptable.

4. Primary Eye Irritation

Conjunctival findings at 24 hours showed redness, chemosis, and discharge. At 48 hours, the cornea and iris of one animal could not be evaluated due to destruction and blanching of the conjunctival tissue; redness, chemosis, and discharge in the treated eye. The study (MRID 50934829) is acceptable, and the proposed product is placed in Toxicity Category I.

5. Primary Skin Irritation

The study report (MRID 50934830) indicated that the proposed product was moderately irritating with well-defined erythema and moderate edema clearing by 72 hours. Eschar was noted on one site at 7 and 10 days. The study is acceptable, and the proposed product is placed in Toxicity Category III.

6. Dermal Sensitization

The study report (MRID 50934831) indicated that the proposed product is a sensitizer. This study is acceptable.

7. The acute toxicity profile of *Neogen Viroxide Super*, EPA Reg. No. 66171-RNA, is currently:

Study	MRID	Toxicity Category	Status
Acute Oral Toxicity	50934826	III	Acceptable
Acute Dermal Toxicity	50934827	IV	Acceptable
Acute Inhalation Toxicity	50934828	III	Acceptable
Primary Eye Irritation	50934829	I	Acceptable
Primary Skin Irritation	50934830	III	Acceptable
Dermal Sensitization	50934831	Sensitizer	Acceptable

III. CONCLUSION

The acute toxicity data requirements have been met to support the registration of EPA Reg. No. 66171-RNA .

IV. PRODUCT LABELING

1. Signal Word: DANGER/PELIGRO

2. The statement, "Keep Out of Reach of Children (KOROC)", is required. It should appear immediately below the front-panel signal word "DANGER".

3. The Agency's *Label Review Manual* (https://www.epa.gov/pesticide-registration/label-review-manual) indicates the following human-hazard precautionary statements, and the Spanish statement must appear as follows:
"Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)"

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS:

DANGER. Corrosive. Causes irreversible eye damage. Harmful if swallowed or inhaled. Do not get in eyes, on skin, or on clothing. Avoid breathing dust. Wear goggles, face shield, or safety glasses. Wear long-sleeved shirt, long pants, socks, shoes, and waterproof gloves. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet. Remove and wash contaminated clothing before reuse. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. The proposed product may cause asthmatic signs and symptoms in hyper-reactive individuals.

Note: The registrant indicates that the proposed product powder is corrosive (pH also shows it's corrosive). The final draft label has Toxicity Category I precautionary statement for eye and skin irritation endpoints and Toxicity Category III precautionary statement for acute dermal toxicity endpoint, which the Agency agrees with the registrant's proposal. Additionally, because the proposed product powder is corrosive and a skin sensitizer, irritation and sensitization of respiratory tract may most likely occur when being exposed to the product powder. A respirator precautionary statement is highly recommended: Wear a NIOSH-approved Wear a minimum of a NIOSH-approved particulate filtering facepiece respirator with any N1 , R, or P filter; OR a NIOSH-approved elastomeric particulate respirator with any N1 , R, or P filter; OR a NIOSH-approved powered air purifying respirator with HE filters.

4. The First Aid statements must state:

IF IN EYES:

- Hold eye open and rinse slowly and gently with water for 15-20 minutes.
- Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
- Call a poison control center or doctor for treatment advice.

IF ON SKIN OR CLOTHING:

- Take off contaminated clothing.

- Rinse skin immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor for treatment advice.

IF SWALLOWED:

- Call a poison control center or doctor immediately for treatment advice.
- Have person sip a glass of water if able to swallow.
- Do not induce vomiting unless told to by a poison control center or doctor.
- Do not give anything by mouth to an unconscious person.

IF INHALED:

- Move person to fresh air.
- If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible.
- Call a poison control center or doctor for further treatment advice.

NOTE TO PHYSICIAN: Probable mucosal damage may contraindicate the use of gastric lavage.

GENERAL INFORMATION: Have the product container or label with you when calling a poison control center or doctor or going for treatment. For non-emergency and general information on product use, etc., information pertaining to this product, call the National Pesticides Information Center at 1-800-858-7378 (NPIC web site: www.npic.orst.edu). For emergencies, call the poison control center 1-800-222-1222.

5. Restricted Use Classification: This product meets the Agency requirements for Restricted-Use Classification based on data that place it in toxicity category I for primary eye and skin irritation. In lieu of assigning the product Restricted-Use classification, the product manager may consider alternatives such as face shield or goggles (to mitigate the identified hazards). Restricted-Use requirements vary depending upon use sites, e.g., institutional use, residential use, etc. Please refer to the 40 CFR §152.170 for information on Restricted-Use products.

6. Based upon data placing it in toxicity category I for primary eye, this product meets the Agency requirements for Child-Resistant Packaging (CRP). However, the Agency

does not require products that are assigned Restricted-Use status to be placed in CRP in addition to Restricted-Use Classification. CRP requirements vary depending upon use sites, e.g., institutional use, residential use, etc. As this is an industrial-use product, it will like require CRP. Please refer to the 40 CFR, §157.22 and 157.24 for CRP requirements and exemptions. Thus, CTT recommends that the Product Manager assign this product Restricted-Use classification; if not, the registrant should place this product in CRP.

DATA REVIEW FOR ACUTE ORAL TOXICITY STUDY (OCSPP 870.1100)

Product Manager: Karen Leavy **Reviewer:** Milutin S. Djurickovic
MRID No.: 50934826 **Study Completion Date:** 3/2/2020
Project No.: 51701

Testing Laboratory: Product Safety Labs (Dayton, New Jersey)
Author: Jennifer Durando, BS

Quality Assurance (40 CFR §160): Included

Test Material: Neogen Viroxide Super (Lot no. RDB1908004) powder
Dose levels: 175, 550, 1750, or 5000 mg/kg bw

Animals: Rat, Sprague-Dawley-derived albino strain
Number/Sex: 9 Females
Age: 8-10 weeks
Weight: 205-255 g
Source: Charles River Laboratories

Method: Up-and-Down Procedure (OECD 425)

Summary:

1. **Estimated LD_{50}:** 3129 mg/kg bw (95% C.L.: 1750-5000 mg/kg bw)
2. **Toxicity Category:** III
3. **Classification:** Acceptable

Deviations from OECD 425 and other comments: The test substance was administered as a 40% w/w mixture in distilled water because it's too viscous to be administered properly at concentrations greater than 40% (>40%).

Procedure: An initial limit test with one female animal at a dose of 5000 mg/kg was conducted. Due to mortality in this animal, a Main Test was proceeded using the default starting dose of 175 mg/kg following the Up and Down procedure (UPD), eight additional females were dosed at levels of 550, 1750, or 5000 mg/kg. Females were selected for the test because they are frequently more sensitive to the toxicity of test compounds than males. All animals were observed for mortality, signs of gross toxicity, and behavioral changes at least once daily for 14 days after dosing or until death occurred. Body weights were recorded prior to administration (initial) and again on Days 7 and 14 (terminal) following dosing or after death. Necropsies were performed on all animals.

Results:

The table below gives the mortality following gavage administration of the undiluted test substance to nine fasted animals at dose levels of 175 mg/kg bw (1 animal), 550 mg/kg bw (1 animal), 1750 mg/kg bw (3 animals), or 5000 mg/kg bw (4 animals, including one used in an initial limit test). Note: dosing sequence, stopping criterion, and LD_{50} calculation were in accordance with AOT425statpgm with default assumed LD_{50} and sigma of 0.5.

175 and 550 mg/kg bw: There were no deaths, abnormal clinical signs, or abnormal gross necropsy findings. Both animals gained weight during both weeks of the study.

1750 mg/kg bw (3 animals): There were no deaths or abnormal gross necropsy findings, and all animals gained weight during both weeks of the study. Two animals exhibited irregular respiration, hypoactivity, hunched or prone posture, reduced fecal volume, anogenital staining, and/or "red staining on the polypad" between Days 0 and 3. Both rats were normal by Day 4 and thereafter. The remaining animal appeared active and healthy throughout the study.

5000 mg/kg bw (4 animals): All animals were found dead within 24 hours of dosing after exhibiting irregular respiration, abnormal gait, hypoactivity, hunched or prone posture, and/or tremors. Abnormal gross findings included the following: extreme stomach distension in 2/4 animals; stomach filled with light green fluid in 1/4 animals; and thickened stomach, black discoloration of the stomach, and mottled tan and black discoloration of the liver in 1/4 animals.

Reported Mortality

Dosing Sequence	Dose Level (mg/kg bw)	Short-Term Outcome	Long-Term Outcome
Limit Test			
1	5000	X	X
Main Test			
1	175	O	O
2	550	O	O
3	1750	O	O
4	5000	X	X
5	1750	O	O
6	5000	X	X
7	1750	O	O
8	5000	X	X

O = Survival; X = Death.

DATA REVIEW FOR ACUTE DERMAL TOXICITY STUDY (OCSPP 870.1200)

Product Manager: Karen Leavy **Reviewer:** Milutin S. Djurickovic
MRID No.: 50934827 **Study Completion Date:** 2/28/2020
Project No.: 51702

Testing Laboratory: Product Safety Labs (Dayton, New Jersey)
Author: Jennifer Durando, BS

Quality Assurance (40 CFR §160): Included

Test Material: Neogen Viroxide Super (Lot no. RDB1908004) powder
Dose level: 5000 mg/kg bw

Animals: Rat, Sprague-Dawley-derived albino strain
Number/sex: 5 males and 5 females
Age: 10 weeks
Weight: Males: 287-298 grams; Females: 226-262 grams
Source: Charles River Laboratories

Summary:

1. **Estimated LD_{50}:** > 5000 mg/kg bw (a limit test)
2. **Toxicity Category:** IV
3. **Classification:** Acceptable

Deviations from Guideline 870.1200 and other comments: The test substance was administered as a dry paste (80% w/w mixture in distilled water). It's too dry to assure adequate skin contact at concentrations greater than 85% (>85%). However, the same test substance was administered at 90% dry paste for the submitted skin irritation test, which is the same route of exposure but at much less contact time, i.e., 4-hour *vs* 24-hour. Additionally, the 2 inch x 3 inch (38.7 cm^2) application site was likely smaller than 10% of the total body surface area (BSA) for all of the male rats. With BSA estimated as 9.83 x (wt in grams)$^{2/3}$, the males were treated over ~8.8% to 9.0% of their BSAs.

Results:

The table below gives the mortality outcomes following a 24-hour dermal exposure of five male and 5 female rats to the test substance applied (Day 0) to previously clipped skin (~2 inches by 3 inches; ~8.8-10.6% of the body surface area) as a dry paste (85% w/w mixture in distilled water) at a dose level of 5000 mg/kg bw. There were no deaths or abnormal gross necropsy findings, and all animals gained weight during both weeks of the study. Abnormal clinical signs were limited to local effects on all dose sites. On

Day 1, all animals had erythema and yellow staining of the dose site, and one animal had dark discoloration of the dose site. Additional findings with later onset were noted on two males and four females, as follows: hyperkeratosis on three animals (Days 2-3); eschar on six animals (from Day 4 through Days 5-7), desquamation on four animals (between Days 6 and 10), and "small areas of superficial eschar" on three animals (between Days 7 and 10). All abnormalities resolved by Day 11.

Reported Mortality

Dose Level (mg/kg bw)	Number Dead / Number Tested		
	Males	Females	Combined
5000	0 / 5	0 / 5	0 / 10

DATA REVIEW FOR ACUTE INHALATION TOXICITY STUDY (OCSPP 870.1300)

Product Manager: Karen Leavy **Reviewer:** Milutin S. Djurickovic
MRID No.: 50934828 **Study Completion Date:** 3/2/2020
Project No.: 51703

Testing Laboratory: Product Safety Labs (Dayton, New Jersey)
Author: Jennifer Durando, BS

Quality Assurance (40 CFR §160): Included

Test Material: Neogen Viroxide Super (Lot no. RDB1908006) powder

Concentrations: Gravimetrically determined: 2.20 mg/L (Nominal: 5.22 mg/L) and 0.56 mg/L (Nominal: 2.33 mg/L)

Chamber Type: Nose-only

Animals: Rat, Sprague-Dawley-derived albino strain
- **Number/sex:** 10 Males and 10 Females
- **Age:** 8-11 weeks
- **Weight:** Males: 237-323 g; Females: 193-235 g
- **Source:** Envigo RMS Inc. and Charles River Laboratories

Method: OCSPP 870.1300; OECD 403 traditional protocol

Summary:

1. **Estimated LC_{50}:** > 0.56 mg/L and < 2.20 mg/L
2. **Mean MMAD:** 2.35 µm (at 2.20 mg/L) and 2.90 µm (at 0.56 mg/L)
3. **Toxicity Category:** III
4. **Classification:** Acceptable

Deviations from Guideline 870.1300 and other comments: Under OCSPP 870.1300, three to four MMAD measurements are to be taken during the actual exposures, unless two MMAD measurements taken during a pre-test trial are within 10% of each other. In this study, MMAD was determined only twice during each exposure, with single MMAD measurements made during the pre-test trials for each concentration. It appears that MMAD was probably consistent during the 2.20 mg/L exposure given that all three values were within ±10% of each other. However, the MMAD measurements during the 0.56 mg/L exposure (3.00 and 1.65 µm) and during a pretest trial at 0.53 mg/L (1.86 µm) were not within ±10% of each other.

Results:

The tables below summarize mortality, chamber atmospheres, and the chamber environments for two four-hour nose-only inhalation exposures to the aerosolized undiluted (ungrounded) test material at mean gravimetric concentrations of 2.20 mg/L (average MMAD: 2.35 µm; GSD: 2.20) or 0.56 mg/L (average MMAD: 2.33 µm; GSD: 2.23), respectively. Exposure was on Day 0, and the animals were observed for up to 14 days.

2.20 mg/L: One male was found dead on Day 3, and the remaining animals were sacrificed on Day 3 for humane reasons (excessive body weight loss and adverse clinical signs). All animals exhibited irregular respiration and moist rales (first noted upon removal from the chamber), followed by gasping and/or hypoactivity (first noted Day 1), with red facial staining noted on two males. At necropsy, all animals had distension of the stomach and intestines and red discoloration of the lungs.

0.56 mg/L: There were no deaths. Four males and five females had moist rales and irregular respiration beginning on Day 1. Recovery occurred on Days 3-9. All animals lost weight during Days 0-1 but gained weight during all subsequent measuring intervals and had cumulative weight gain for Days 0-14. There were no abnormal gross necropsy findings.

Reported Mortality

Exposure Concentration (mg/L)	Number dead / Number tested		
	Males	Females	Combined
2.20	5 / 5	5 / 5	10 / 10
0.56	0 / 5	0 / 5	0 / 10

Chamber Atmosphere

Exposure Conc. (mg/L)	Mean MMAD (µm)	GSD
2.20±0.17 [Range: 2.05-2.48]	2.35 [2.35, 2.34]	2.20 [2.33, 2.06]
0.56±0.10 [Range: 0.43-0.73]	2.33 [3.00, 1.65]	2.23 [2.40, 2.05]

Chamber Environment

Exposure Level (mg/L)	2.20	0.56
Chamber Volume (L)	28	28
Total Airflow Rate (Lpm)	56.0	60.0
Temperature (°C)	20-21	20-22
Relative Humidity (%)	42-44	41-51
T_{99} value (minutes)	2.30	2.15

DATA REVIEW FOR ACUTE EYE IRRITATION STUDY (OCSPP 870.2400)

Product Manager: Karen Leavy
Reviewer: Milutin S. Djurickovic
MRID No.: 50934829
Study Completion Date: 2/28/2020
Report No.: 51704

Testing Laboratory: Product Safety Labs (Dayton, New Jersey)
Author: Jennifer Durando, BS

Quality Assurance (40 CFR §160): Included

Test Material: Neogen Viroxide Super (Lot no. RDB1908004) powder
Dosage: 0.10 g

Species: Rabbit, New Zealand albino strain
Number/Sex: Three female
Age: 13 weeks
Weight: 2998-3139 g
Source: Robinson Services, Inc.

Summary:

1. **Toxicity Category:** I
2. **Classification:** Acceptable

Deviations from OCSPP 870.2400 and other comments: Classification of the test material in EPA Toxicity Category I is based on the study author's statement that the test substance caused irreversible destruction of the ocular tissue. This appears to be true of one animal. The animal's individual findings at 48 hours included "destruction and blanching of the conjunctival tissue" and a statement that the globe of the eye was not visible; the destruction was not further characterized (e.g. as ulceration, sloughing, necrosis), and the extent of the blanching was not described. The lesions in the remaining two animals were not severe (i.e. they were not "predictive of severe irritant or corrosive injuries and injuries that are not expected to fully reverse by the end of the 21-day observation period") according to the criteria given in OECD 405 (2017). The Reviewer notes that it is currently strongly recommended that the *in vivo* eye irritation test be performed initially using one animal, and that observations should allow for determination of severity and reversibility before proceeding to a confirmatory test in a second animal.

Results:

The tables below provide the results ("positive" irritation and total Draize scores) following instillation of 0.10 g of the test material into the anesthetized (with Tetracaine) right eye of three rabbits, with the anesthetized but otherwise untreated contralateral eye serving as a control. Note: appropriate preemptive systemic analgesia was also provided.

Findings one hour post instillation consisted of conjunctival redness (scores=1), chemosis (scores=2), and discharge (scores=2-3). At 24 hours, corneal opacity was noted in 3/3 eyes (scores=2) and involved greater than 75% of the surface and up to the whole area in 1/3 eyes. Conjunctival findings at 24 hours had worsened such that the redness, chemosis, and discharge were scored as 2, 4, and 3, respectively (with the same scores noted in all eyes). At 48 hours, the cornea and iris of one animal could not be evaluated due to destruction and blanching of the conjunctival tissue; redness, chemosis, and discharge in the treated eye of this animal were scored as 3, 4, and 3, respectively, and the discharge was red in color. The 48-hour findings in the remaining two animals consisted of corneal opacity (score=1) and conjunctival redness, chemosis, and discharge (scores of 2, 4, and 3, respectively). The study author stated, "Due to the severity of scores noted in the treated eyes of all three animals at 48 hours, the study was terminated and the animals were euthanized for humane reasons." The study author concluded that the test substance caused irreversible destruction of the ocular tissue. Because of the early termination, the Reviewer has not determined a descriptive classification (per Kay and Calandra). There were no abnormal systemic clinical signs. The three animals had small weight losses (13-52 g) during the 2-day study; these cannot be attributed to treatment because the animals were not fed *ad libitum*.

Observations	**Number "Positive" / Number Tested**			
	Time After Instillation			
	Hours			
	1	**24**	**48**	**72**
Corneal Opacity	0/3	3/3	1/2 [a]	-- [b]
Iritis	0/3	0/3	0/2 [a]	--
Conjunctivae				
Redness *	0/3	3/3	3/3	--
Chemosis *	3/3	3/3	3/3	--
Discharge**	3/3	3/3	3/3 [c]	--
Severity of Irritation: Mean Total Score	11.3	41.3	-- [a]	--

* Score of 2 or more required to be considered "positive."

** Not considered a positive irritation effect; however, scores of 2 or greater are noted here for completeness.

[a] The cornea and iris of one animal could not be evaluated due to destruction and blanching of the conjunctival tissue.
[b] The study was terminated ahead of schedule at 48 hours.
[c] Red discharge was seen in one animal.

DATA REVIEW FOR ACUTE DERMAL IRRITATION STUDY (OCSPP 870.2500)

Product Manager: Karen Leavy
Reviewer: Milutin S. Djurickovic
MRID No.: 50934830
Study Completion Date: 1/23/2020
Project No.: 51705

Testing Laboratory: Product Safety Labs (Dayton, New Jersey)
Author: Jennifer Durando, BS

Quality Assurance (40 CFR §160): Included

Test Material: Neogen Viroxide Super (Lot no. RDB1908004) powder
Dosage: 0.5 mL

Animals: Rabbit, New Zealand White strain
Number/Sex: 3 Females
Age: 11-13 weeks
Weight: 2586-2894 g
Source: Robinson Services Inc.

Summary:

1. **Toxicity Category:** III
2. **Classification:** Acceptable

Deviations from Guideline 870.2500 and/or other comments: The test substance was administered as a dry paste (90% w/w mixture in distilled water) because it's too viscous to assure adequate skin contact at concentrations greater than 90%. Although moderate irritation (erythema) was not seen on any dose site at 72 hours, the presence of eschar (injury in depth) 7 and 10 days after treatment warrants classification in EPA Toxicity Category III rather than EPA Toxicity Category IV.

Results:

The table below provides the results (Draize scores) after a four-hour dermal exposure of three rabbits to 0.5 g of the test material, applied as a dry paste (90% w/w/ mixture in distilled water) to intact clipped application sites measuring ~ 6 cm^2 and covered semi-occlusively. At 30-60 minutes after patch removal, the three sites exhibited well-defined erythema, slight or moderate edema, and dark discoloration, with blanching noted on 2/3 sites. At 24 hours, moderate to severe erythema was present on one site, well-defined erythema was present on the other two sites, slight edema and dark discoloration were noted on all sites, and blanching was noted on one site. Thereafter the skin irritation generally decreased in incidence and severity over time, except eschar

was noted on one site at 7 and 10 days (with very slight erythema and edema also present on this site). The skin abnormalities resolved by Day 7 on one animal and by Day 14 on the remaining two animals. Two animals lost weight during the study (143-176 g); this cannot be attributed to treatment because the animals were not fed *ad libitum*. No abnormal systemic clinical signs were recorded. In this study the Primary Dermal Irritation Index was 3.9, making the test material a *moderate irritant* (US EPA, 1988).

Individual Dermal Irritation Scores following the four-hour exposure

Animal No.	Sex	Erythema/Edema						
		Time After Patch Removal						
		30-60 min	24 hrs	48 hrs	72 hrs	7 days	10 days	14 days
3501	F	2 / 3 [a b]	2 / 2 [a]	1 / 1 [a]	1 / 1 [a]	0 / 0	-- [c]	--
3502	F	2 / 2 [a]	2 / 2 [a]	2 / 2 [a]	2 / 2 [a]	1 / 1	1 / 1	0 / 0
3503	F	2 / 2 [a b]	3 / 2 [a b]	3 / 2 [a]	2 / 2 [a]	1 / 1 [d]	1 / 1 [d]	0 / 0

[a] Dark discoloration present on dose site.

[b] Blanching at the dose site.

[c] The animal was removed from the study after Day 7.

[d] Eschar at the dose site.

DATA REVIEW FOR DERMAL SENSITIZATION STUDY (OCSPP 870.2600)

Product Manager: Karen Leavy **Reviewer:** Milutin S. Djurickovic
MRID No.: 50934831 **Study Completion Date:** 1/23/2020
Project No.: 51706

Testing Laboratory: Product Safety Labs (Dayton, New Jersey)
Author: Jennifer Durando, BS

Quality Assurance (40 CFR §160): Included

Test Material: Neogen Viroxide Super (Lot no. RDB1908004) powder
Inductions: 0.4 g of an 85% w/w mixture of the test item in distilled water
Challenge: 0.4 mL of a 21% w/w mixture of the test item in distilled water
Animals: Guinea pig, Hartley albino strain
Test group: 20 Males
Naive control: 10 Males
Preliminary test: 4 Males
Age: "Young adult" (exact age not specified)
Weight: 368-442 grams (test group and naïve controls)
Source: Elm Hill Breeding Labs
Historical Positive Control Study: alpha-Hexylcinnamaldehyde (HCA)
Guinea pig, Hartley albino; 19 males
Induction: 0.4 mL of undiluted HCA
Challenge: 0.4 mL of undiluted HCA
Conducted 8/6/2019 to 9/5/2019 (within 6 months of the current study)

Method: Buehler

Summary:

1. In this study, Neogen Viroxide Super *was* a sensitizer.
2. **Classification:** Acceptable

Deviations from Guideline 870.2600: The ages of the animals were not provided.

Procedure Highlights:

- The materials were applied to clipped skin using a Hill Top Chamber.

- Exposure periods: 6 hours; Observations: 24 and 48 hours after application.
- Inductions: once/week for three weeks (left side); Challenge: 28 days after first dose (right side).
- Due to the severity of the irritation resulting from the inductions, a different naïve area was used for each induction.

Results:

The results are given in the tables below. Following the first two inductions, all of the sites exhibited very faint or faint erythema (scores of 0.5 or 1) at both 24 and 48 hours. Following the third induction, all of the sites exhibited faint or moderate erythema (scores of 1 or 2) at both 24 and 48 hours. Following challenge, positive scores (of 1 or 2) were noted on 18/20 and 19/20 treated animals at 24 and 48 hours, respectively. Additionally, very faint erythema was noted on 2/20 and 1/20 test animals at the same respective time points. Findings on naïve controls were limited to very faint erythema on 4/10 and 2/10 animals at 24 and 48 hours, respectively.

Results for the historical positive controls were appropriate.

Response Indices - Erythema at Challenge – Neogen Viroxide Super

Group	Incidence of Positive Response[1]		Severity[2]	
	24 Hrs	48 Hrs	24 Hrs	48 Hrs
Test Group	18 / 20	19 / 20	1.10	1.43
Naïve Control Group	0 / 10	0 / 10	0.20	0.10

[1] Number of erythema scores greater than 0.5 per number of animals evaluated.
[2] Sum of the erythema scores divided by the number of animals evaluated.

Skin Reaction Scores (Erythema) – Neogen Viroxide Super

		Induction						Challenge	
		1		2		3			
Hours after dose		24	48	24	48	24	48	24	48
Animal	Sex								
Test Group									
3601	M	1	1	1	1	1	1	1	1
3602	M	1	1	1	0.5	1	1	1	2
3603	M	1	1	1	1	1	2	1	1
3604	M	1	1	0.5	0.5	1	2	1	1
3605	M	1	1	1	0.5	1	2	1	1
3606	M	0.5	0.5	1	0.5	1	2	0.5	1
3607	M	1	1	1	0.5	1	2	1	2
3608	M	1	1	0.5	0.5	1	2	1	1
3609	M	1	1	1	1	1	1	2	2
3610	M	1	1	0.5	0.5	2	2	0.5	0.5
3611	M	1	1	1	1	1	2	2	2
3612	M	1	1	1	1	1	2	1	1
3613	M	1	1	1	1	2	2	2	2
3614	M	1	1	1	1	2	2	1	1
3615	M	1	1	1	1	2	2	1	2
3616	M	1	1	1	0.5	2	2	1	2
3617	M	1	1	1	0.5	2	2	1	1
3618	M	1	1	1	1	2	2	1	2
3619	M	1	1	1	0.5	2	2	1	2
3620	M	1	1	1	0.5	2	2	1	1
Naïve Control Group									
3621	M	--	--	--	--	--	--	0.5	0
3622	M	--	--	--	--	--	--	0	0
3623	M	--	--	--	--	--	--	0	0
3624	M	--	--	--	--	--	--	0.5	0.5
3625	M	--	--	--	--	--	--	0	0
3626	M	--	--	--	--	--	--	0.5	0.5
3627	M	--	--	--	--	--	--	0	0
3628	M	--	--	--	--	--	--	0	0
3629	M	--	--	--	--	--	--	0	0
3630	M	--	--	--	--	--	--	0.5	0